Derivation of Plasma Concentration (Urea, Creatinine, Uric Acid) from Dialysate Concentration and Blood Flow in Two Types of Kiil Haemodialyzer (with Nomograms)


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Regular haemodialysis is able to abolish many symptoms of terminal renal failure. An abnormality which is not, or only imperfectly, corrected is anaemia. Since this anaemia is mainly aplastic in nature, it is enhanced by regular withdrawal of even small quantities of blood. In considering ways to reduce the quantity of blood for the chemical control of regular haemodialysis, we decided to examine whether, and, if so, with what degree of accuracy, the plasma concentration of the patient could be derived from the dialysate concentration. The present study concerned the relationship between these parameters, for two commercial types of Kiil haemodialyzer and for the substances urea, creatinine, and uric acid.

MATERIALS AND METHODS

The two types of Kiil haemodialyzer used in the study will here be called type A and type B. Nine dialyzers of type A (Internal gasket haemodialyzer with clamp, Sweden Artificial Kidney Supply Company, Seattle (Wash.) USA) and ten of type B (Dasco haemodialyzer, Dasco Laboratories, Mirandola, Italy) were investigated. Cuprophane PT 150 membranes (Bemerg Wuppertal, supplied by Sweden Artificial Kidney Supply Company, Seattle (Wash.) USA) were applied wet, and were clamped under a torque of 1.2 kg.m. The dialysate and the blood flowed countercurrently. For the dialysate the flow was 500 ml per minute, and the temperature between 37 and 39°C. Blood flow was determined by measuring, with two photo-electric cells and an electronic recorder, the time required for an occluding air bubble of about 0.4 ml to pass through part of the outflow tubing.

At least one hour after connection of the patient to the dialyzer, dialysate was collected for 30 minutes in a container placed 75 cm below the haemo-
dialyzer. Blood samples were taken from the inflow tubing at the beginning and end of the collection period. During this period, three measurements of blood flow were performed. Concentrations were averaged to a geometric, flows to an arithmetic mean.

Urea and creatinine were determined in a continuous-flow system using the urease and the alkaline picrate principles, respectively. Uric acid was determined by spectrophotometry with uricase. The assays were done without special precautions in the routine work of the clinical laboratory and over the period of one year.

MATHEMATICAL CONSIDERATIONS

Figure 1 gives a model of the process of dialysis. The magnitudes concerned are:

- $c_x$: concentration in dialysate at point $x$ ($x$ from left to right)
- $c_y$: concentration in blood at point $y$ ($y$ from right to left)
- $\dot{V}_d$: dialysate flow
- $V_b$: blood flow
- $b$: width of the dialyzer
- $l$: length of the dialyzer
- $S$: dialyzing surface (equal to $4bl$ in the two-layer Kiil)
- $k$: effective permeability constant

![Figure 1. Model of the dialysis process](image)

For a diffusible substance not present in the inflowing dialysate, the following three equations can be given:

\[
(1) \quad \frac{dc_x}{dx} = \frac{4bk}{V_b} \frac{(c_y - c_x)}{dy}
\]

\[
(2) \quad \frac{dc_y}{dy} = \frac{-4bk}{V_b} \frac{(c_x - c_y)}{dx}
\]
Solutions of equations (1) and (2), under the requirement that the amount removed from the blood is equal to the amount appearing in the dialysate, and for \( y = 0 \) and \( x = 1 \), gives:

\[
(3) \quad f = \frac{c_y = 0}{c_x = 1} = \frac{kS \left[ \frac{1}{V_b} - \frac{1}{V_d} \right]}{e} - 1
\]

Equation (3) leads to the conclusion that \( f \), the relation between the concentrations of the inflowing blood and the outflowing dialysate, is an exponential function of blood flow, dialysate flow, and a term \( kS \), determined by the effective membrane permeability and the effective contact area. If the magnitudes in the right hand side of equation (3) are known, one can calculate blood concentration from dialysate concentration. If, on the other hand, flows and concentrations are known, one can compute \( kS \), which is characteristic for the physical properties of the dialyzer. For this purpose, equation (3) may be written as:

\[
(4) \quad kS = \frac{V_d}{V_b} \ln \frac{f - 1}{f - \frac{V_d}{V_b}}
\]

The derivation of blood concentration from dialysate concentration and blood flow can be simplified by the construction of nomograms. For this construction, the following considerations can be given with reference to Figure 2.

If the scale on axis a is taken \( \frac{p + q}{q} \) times, and the scale on axis c is \( \frac{p + q}{p} \) times, the scale on axis b, one can read the sum of a and c at the point where a line connecting values on a and c, crosses b.

This principle can be applied to:

\[
(1b) \quad f = \frac{c_y = 0}{c_x = 1}
\]

\[
(2b) \quad c_y = 0 = f \cdot c_x = 1
\]

Taking the logarithm of both sides, we get:

\[
(3b) \quad \ln c_y = 0 = \ln f + \ln c_x = 1
\]
If $kS$ and $\dot{V}_d$ are known and constant, equation (3) gives a relation between $f$ and $\dot{V}_b$. This relation enables us to substitute $\ln \dot{V}_b$ for $\ln f$. Nomograms can then be constructed with properly chosen logarithmic scales, on which the concentration of inflowing blood can be read by linear connection of known values for dialysate concentration and blood flow.

RESULTS

Table I gives values for $kS$ obtained by simultaneous determinations of blood and dialysate concentrations and blood flows at a constant dialysate flow of 500 ml per minute, for the two Kill types and the three substances examined.

<table>
<thead>
<tr>
<th>Substance</th>
<th>Kiil type A</th>
<th>Kiil type B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>number of observations</td>
<td>$kS$</td>
</tr>
<tr>
<td>urea</td>
<td>62</td>
<td>100.3 ± 29.7</td>
</tr>
<tr>
<td>creatinine</td>
<td>78</td>
<td>69.5 ± 11.4</td>
</tr>
<tr>
<td>uric acid</td>
<td>25</td>
<td>56.4 ± 9.5</td>
</tr>
</tbody>
</table>
The differences between the means for the two Kill types were significant (P<0.001). Since the same cellophane was used for both series, it may be concluded that the effective dialyzing surface of type B is about 17% smaller than that of type A.

Figure 3 shows curves relating $\frac{c_{y=0}}{c_{x=1}}$ to $\dot{V}_b$ as calculated with the mean values for $k_s$.

Figures 4 and 5 give nomograms for the three substances under consideration, for the Kill types A and B.

In order to elucidate the accuracy of the derivation procedure, Figure 6 gives in bissectrix diagrams the relations between derived and measured concentrations. The shaded areas in those figures are 95% confidence limits around the regression lines. The standard error of estimate was less than 10% of the maximal values.

**DISCUSSION**

The method presented here offers a simple test for checking the performance of a dialysis system. If a known type of cellophane is used and, where necessary, correction is made for the geometric surface of the dialyzer, this method will provide information about the effective area available for dialysis. Where the effective surface is known, the effective permeability of the membranes can be studied on a comparative basis.

![Diagram](image)

Figure 3. The relation of $\frac{c_{y=0}}{c_{x=1}}$ to $\dot{V}_b$ for Kill types A and B, and for urea, creatinine, and uric acid.
Figure 4. Nomograms for the derivation of plasma concentration (urea, creatinine, and uric acid) from dialysate concentration and blood flow in Kill type A. By linear connection of the two latter values, the former can be read off from the middle axis.

Figure 5. Nomograms for the derivation of plasma concentration (urea, creatinine, and uric acid) from dialysate concentration and blood flow in Kill type B. By linear connection of the two latter values, the former can be read off from the middle axis.
Although the substances examined in this study are not similarly distributed over the plasma and erythrocytes, such differences in distribution will change blood flow into the flow of a hypothetical carrier for the substance under consideration. But since kS is independent of blood flow, it will remain independent of the actual flow of this carrier.

The nomograms derive their value from empirical data. It is conceivable, however, that their accuracy for substances unequally distributed over plasma and erythrocytes could be increased by introducing a correction for the haematocrit. We have not done so, because the haematocrit of patients with terminal renal failure is rather uniform, whereas correction for it would have required a three-compartment model and would have introduced a number of uncertainties.

The inaccuracy of the nomogram reading is the sum of all inaccuracies in the procedure, including those of the measurements of blood flow, the geometrical differences between the individual dialyzers, the laboratory assay, and the reading of the nomogram itself. It depends, of course, upon the objective of the control whether or not this inaccuracy will be considered acceptable. The saving of blood depends on the laboratory technique employed...
for the determination in blood, and the frequency of control considered necessary. In our unit the method was found to save 10 to 15 ml of blood per dialysis.

For us at least, this seems to give ample compensation for the lower degree of accuracy in routine regular haemodialysis.

SUMMARY

From the mathematical relation between the concentrations and flow rates of the inflowing blood and outflowing dialysate in a haemodialyzer, a constant can be derived, determined by effective membrane permeability and dialyzing surface. This constant being known for a specific type of dialyzer, the concentration of a diffusable substance in the inflowing blood can be derived from the concentration of the outflowing dialysate and the blood flow, at a fixed dialysate flow. This derivation can be simplified by the construction of nomograms. The present study provides data and nomograms for two types of Kiil haemodialyzer and for the substances urea, creatinine, and uric acid.